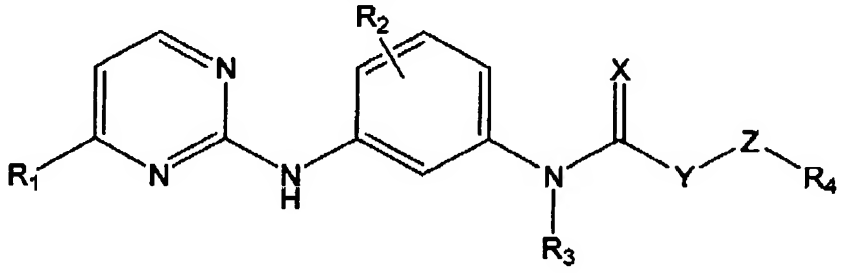
Application Number: 10/821,382

Amendments on the original claims

What is claimed is:

1. A phenylaminopyrimidine ~~derivative~~ *compound (35 U.S.C. 112)* of formula (I)



Formula (I)

Wherein

X is oxygen or sulfur,

Y is a direct bond, oxygen, nitrogen or lower alkyl,

Z is an aliphatic, cycloaliphatic, aryl or a heterocyclyl radical,

R_1 is heterocyclyl radical,

R_2 is hydrogen, halogen, halogenlower alkyl, lower alkyl or lower alkoxyl,

R_3 is hydrogen or lower alkyl,

R_4 is oxy-lower alkylamino, lower alkyl oxy-lower alkylamino, oxyheterocyclyl, lower alkyl oxyheterocyclyl, oxy-lower alkylheterocyclyl, lower alkyl oxy-lower alkylheterocyclyl, halogenlower alkylamino, halogenlower alkylheterocyclyl, ~~amino lower alkylamino,~~ *(35 U.S.C. 102, 35 U.S.C. 103)* lower alkylamino lower alkylamino,

aminoheterocyclyl *with the proviso that heterocyclyl defined herein is not selected from N-lower alkylpyrrolidinyl or N-lower alky piperidinyl, (35 U.S.C. 102, 35 U.S.C. 103)*

lower alkylamino heterocyclyl *with the proviso that lower alkyamino defined herein is not para-substituted* with *–CH_2NH– when Z is the phenyl ring, (35 U.S.C. 102, 35 U.S.C. 103)*

amino lower alkylheterocyclyl or lower alkylamino lower alkylheterocyclyl,

or a pharmaceutically acceptable salt thereof.

2. A compound of Formula (I) according to claim 1, wherein

X is oxygen or sulfur,

Y is a direct bond, oxygen, nitrogen or lower alkyl,

Z is an aliphatic, cycloaliphatic, aryl or a heterocyclyl radical,

R_1 is heterocyclyl radical,

R_2 is hydrogen, halogen, halogenlower alkyl, lower alkyl or lower alkoxyl,

R_3 is hydrogen or lower alkyl,

R_4 is:

(a) oxy-lower alkyl unsubstituted, mono or disubstituted amino; oxy-lower alkyl morpholinyl, oxy-lower alkyl pyrrolidinyl, oxy-lower alkyl piperidinyl, oxy-lower alkyl piperazinyl, ~~oxy-lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)* oxy-pyrrolidinyl, oxy-piperidinyl,

(b) lower alkyl oxy-lower alkyl unsubstituted, mono or disubstituted amino; lower alkyl oxy-lower alkyl morpholinyl, lower alkyl oxy-lower alkyl pyrrolidinyl, lower alkyl oxy-lower alkyl piperidinyl, lower alkyl oxy-lower alkyl piperazinyl, ~~lower alkyl oxy-lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)* lower alkyl oxy-pyrrolidinyl, lower alkyl oxy-piperidinyl,

(c) mono or difluoro substituted lower alkyl unsubstituted, mono or disubstituted amino; mono or difluoro substituted lower alkyl morpholinyl, mono or difluoro substituted lower alkyl pyrrolidinyl, mono or difluoro substituted lower alkyl piperidinyl, mono or difluoro substituted lower alkyl piperazinyl, ~~mono or difluoro substituted lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)*

(d)~~ amino lower alkyl unsubstituted, mono or disubstituted amino;~~ amino lower alkyl morpholinyl, amino lower alkyl pyrrolidinyl, amino lower alkyl piperidinyl, amino lower alkyl piperazinyl,~~ amino lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)*

amino pyrrolidinyl, amino piperidinyl *with the proviso that pyrrolidinyl or piperidinyl defined herein is not selected from N-lower alkylpyrrolidinyl or N-lower alky piperidinyl, (35 U.S.C. 102, 35 U.S.C. 103)*

(e) lower alkylamino lower alkyl unsubstituted, mono or disubstituted amino; lower alkylamino lower alkyl morpholinyl, lower alkylamino lower alkyl pyrrolidinyl,

lower alkylamino lower alkyl piperidinyl, lower alkylamino lower alkyl piperazinyl, ~~lower alkylamino lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)*

lower alkylamino heterocyclyl *with the proviso that lower alkyamino defined herein is not para-substituted* with *–CH_2NH– when Z is the phenyl ring, (35 U.S.C. 102, 35 U.S.C. 103)*

or a pharmaceutically acceptable salt thereof.

3. A compound of Formula (I) according to claim 1, wherein

X is oxygen or sulfur,

Y is a direct bond,

Z is an aliphatic, cycloaliphatic, aryl or a heterocyclyl radical,

R_1 is heterocyclyl radical,

R_2 is hydrogen, halogen, halogenlower alkyl, lower alkyl or lower alkoxyl,

R_3 is hydrogen or lower alkyl,

R_4 is:

(a) oxy-lower alkyl unsubstituted, mono or disubstituted amino; oxy-lower alkyl morpholinyl, oxy-lower alkyl pyrrolidinyl, oxy-lower alkyl piperidinyl, oxy-lower alkyl piperazinyl, ~~oxy-lower alkyl-aminopyridinyl,~~ *(35 U.S.C. 112)* oxy-pyrrolidinyl, oxy-piperidinyl,

(b) lower alkyl oxy-lower alkyl unsubstituted, mono or disubstituted amino; lower alkyl oxy-lower alkyl morpholinyl, lower alkyl oxy-lower alkyl pyrrolidinyl, lower alkyl oxy-lower alkyl piperidinyl, lower alkyl oxy-lower alkyl piperazinyl, ~~lower alkyl oxy-lower alkyl-aminopyridinyl,~~ *(35 U.S.C. 112)* lower alkyl oxy-pyrrolidinyl, lower alkyl oxy-piperidinyl,

(c) mono or difluoro substituted lower alkyl unsubstituted, mono or disubstituted amino; mono or difluoro substituted lower alkyl morpholinyl, mono or difluoro substituted lower alkyl pyrrolidinyl, mono or difluoro substituted lower alkyl piperidinyl, mono or difluoro substituted lower alkyl piperazinyl, ~~mono or difluoro substituted lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)*

(d) ~~amino lower alkyl unsubstituted, mono or disubstituted amino;~~ amino lower alkyl morpholinyl, amino lower alkyl pyrrolidinyl, amino lower alkyl piperidinyl, amino lower alkyl piperazinyl, ~~amino lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)*

amino pyrrolidinyl, amino piperidinyl *with the proviso that pyrrolidinyl or piperidinyl defined herein is not selected from N-lower alkylpyrrolidinyl or N-lower alky piperidinyl, (35 U.S.C. 102, 35 U.S.C. 103)*

(e) lower alkylamino lower alkyl unsubstituted, mono or disubstituted amino; lower alkylamino lower alkyl morpholinyl, lower alkylamino lower alkyl pyrrolidinyl, lower alkylamino lower alkyl piperidinyl, lower alkylamino lower alkyl piperazinyl, ~~lower alkylamino lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)*

lower alkylamino heterocyclyl *with the proviso that lower alkyamino defined herein is not para-substituted* with *–CH_2NH– when Z is the phenyl ring, (35 U.S.C. 102, 35 U.S.C. 103)*

or a pharmaceutically acceptable salt thereof.

4. A compound of Formula (I) according to claim 1, wherein

X is oxygen or sulfur,

Y is a direct bond,

Z is aryl,

R_1 is heterocyclyl radical,

R_2 is hydrogen, halogen, halogenlower alkyl, lower alkyl or lower alkoxyl,

R_3 is hydrogen or lower alkyl,

R_4 is:

(a) oxy-lower alkyl unsubstituted, mono or disubstituted amino; oxy-lower alkyl morpholinyl, oxy-lower alkyl pyrrolidinyl, oxy-lower alkyl piperidinyl, oxy-lower alkyl piperazinyl, ~~oxy-lower alkyl-aminopyridinyl,~~ *(35 U.S.C. 112)* oxy-pyrrolidinyl, oxy-piperidinyl,

(b) lower alkyl oxy-lower alkyl unsubstituted, mono or disubstituted amino; lower alkyl oxy-lower alkyl morpholinyl, lower alkyl oxy-lower alkyl pyrrolidinyl, lower alkyl oxy-lower alkyl piperidinyl, lower alkyl oxy-lower alkyl piperazinyl, ~~lower-alkyl-oxy-lower-alkyl-aminopyridinyl,~~ *(35 U.S.C. 112)* lower alkyl oxy-pyrrolidinyl, lower alkyl oxy-piperidinyl,

(c) mono or difluoro substituted lower alkyl unsubstituted, mono or disubstituted amino; mono or difluoro substituted lower alkyl morpholinyl, mono or difluoro substituted lower alkyl pyrrolidinyl, mono or difluoro substituted lower alkyl piperidinyl,

mono or difluoro substituted lower alkyl piperazinyl, ~~mono or difluoro substituted lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)*

(d) ~~amino lower alkyl unsubstituted, mono or disubstituted amino;~~ amino lower alkyl morpholinyl, amino lower alkyl pyrrolidinyl, amino lower alkyl piperidinyl, amino lower alkyl piperazinyl, ~~amino lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)*

amino pyrrolidinyl, amino piperidinyl *with the proviso that pyrrolidinyl or piperidinyl defined herein is not selected from N-lower alkylpyrrolidinyl or N-lower alky piperidinyl, (35 U.S.C. 102, 35 U.S.C. 103)*

(e) lower alkylamino lower alkyl unsubstituted, mono or disubstituted amino; lower alkylamino lower alkyl morpholinyl, lower alkylamino lower alkyl pyrrolidinyl, lower alkylamino lower alkyl piperidinyl, lower alkylamino lower alkyl piperazinyl, ~~lower alkylamino lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)*

lower alkylamino heterocyclyl *with the proviso that lower alkyamino defined herein is not para-substituted* with *–CH_2NH– when Z is the phenyl ring, (35 U.S.C. 102, 35 U.S.C. 103)*

or a pharmaceutically acceptable salt thereof.

5. A compound of Formula (I) according to claim 1, wherein

X is oxygen or sulfur,

Y is a direct bond,

Z is aryl,

R_1 is heterocyclyl radical,

R_2 is halogenlower alkyl or lower alkyl,

R_3 is hydrogen or lower alkyl,

R_4 is:

(a) oxy-lower alkyl unsubstituted, mono or disubstituted amino; oxy-lower alkyl morpholinyl, oxy-lower alkyl pyrrolidinyl, oxy-lower alkyl piperidinyl, oxy-lower alkyl piperazinyl, ~~oxy-lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)* oxy-pyrrolidinyl, oxy-piperidinyl,

(b) lower alkyl oxy-lower alkyl unsubstituted, mono or disubstituted amino; lower alkyl oxy-lower alkyl morpholinyl, lower alkyl oxy-lower alkyl pyrrolidinyl, lower alkyl oxy-lower alkyl piperidinyl, lower alkyl oxy-lower alkyl piperazinyl, ~~lower alkyl oxy-~~

~~lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)* lower alkyl oxy-pyrrolidinyl, lower alkyl oxy-piperidinyl,

(c) mono or difluoro substituted lower alkyl unsubstituted, mono or disubstituted amino; mono or difluoro substituted lower alkyl morpholinyl, mono or difluoro substituted lower alkyl pyrrolidinyl, mono or difluoro substituted lower alkyl piperidinyl, mono or difluoro substituted lower alkyl piperazinyl, ~~mono or difluoro substituted lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)*

(d) ~~amino lower alkyl unsubstituted, mono or disubstituted amino;~~ amino lower alkyl morpholinyl, amino lower alkyl pyrrolidinyl, amino lower alkyl piperidinyl, amino lower alkyl piperazinyl, ~~amino lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)*

amino pyrrolidinyl, amino piperidinyl *with the proviso that pyrrolidinyl or piperidinyl defined herein is not selected from N-lower alkylpyrrolidinyl or N-lower alky piperidinyl, (35 U.S.C. 102, 35 U.S.C. 103)*

(e) lower alkylamino lower alkyl unsubstituted, mono or disubstituted amino; lower alkylamino lower alkyl morpholinyl, lower alkylamino lower alkyl pyrrolidinyl, lower alkylamino lower alkyl piperidinyl, lower alkylamino lower alkyl piperazinyl, ~~lower alkylamino lower alkyl aminopyridinyl,~~ *(35 U.S.C. 112)*

lower alkylamino heterocyclyl *with the proviso that lower alkyamino defined herein is not para-substituted* with *–CH_2NH– when Z is the phenyl ring. (35 U.S.C. 102, 35 U.S.C. 103)*

or a pharmaceutically acceptable salt thereof.

6. A compound of Formula (I) according to claim 1, wherein

X is oxygen or sulfur,

Y is a direct bond,

Z is aryl,

R_1 is heterocyclyl radical,

R_2 is lower alkyl,

R_3 is hydrogen,

R_4 is:

(a) oxy-lower alkyl unsubstituted, mono or disubstituted amino; oxy-lower alkyl morpholinyl, oxy-lower alkyl pyrrolidinyl, oxy-lower alkyl piperidinyl, oxy-lower alkyl

piperazinyl, ~~oxy-lower-alkyl-aminopyridinyl,~~ *(35 U.S.C. 112)* oxy-pyrrolidinyl, oxy-piperidinyl,

(b) lower alkyl oxy-lower alkyl unsubstituted, mono or disubstituted amino; lower alkyl oxy-lower alkyl morpholinyl, lower alkyl oxy-lower alkyl pyrrolidinyl, lower alkyl oxy-lower alkyl piperidinyl, lower alkyl oxy-lower alkyl piperazinyl, ~~lower-alkyl-oxy-lower-alkyl-aminopyridinyl,~~ *(35 U.S.C. 112)* lower alkyl oxy-pyrrolidinyl, lower alkyl oxy-piperidinyl,

(c) mono or difluoro substituted lower alkyl unsubstituted, mono or disubstituted amino; mono or difluoro substituted lower alkyl morpholinyl, mono or difluoro substituted lower alkyl pyrrolidinyl, mono or difluoro substituted lower alkyl piperidinyl, mono or difluoro substituted lower alkyl piperazinyl, ~~mono-or-difluoro-substituted-lower-alkyl-aminopyridinyl,~~ *(35 U.S.C. 112)*

(d) ~~amino-lower-alkyl-unsubstituted, mono-or-disubstituted-amino;~~ amino lower alkyl morpholinyl, amino lower alkyl pyrrolidinyl, amino lower alkyl piperidinyl, amino lower alkyl piperazinyl, ~~amino-lower-alkyl-aminopyridinyl,~~ *(35 U.S.C. 112)*

amino pyrrolidinyl, amino piperidinyl *with the proviso that pyrrolidinyl or piperidinyl defined herein is not selected from N-lower alkylpyrrolidinyl or N-lower alky piperidinyl, (35 U.S.C. 102, 35 U.S.C. 103)*

(e) lower alkylamino lower alkyl unsubstituted, mono or disubstituted amino; lower alkylamino lower alkyl morpholinyl, lower alkylamino lower alkyl pyrrolidinyl, lower alkylamino lower alkyl piperidinyl, lower alkylamino lower alkyl piperazinyl, ~~lower-alkylamino-lower-alkyl-aminopyridinyl,~~ *(35 U.S.C. 112)*

lower alkylamino heterocyclyl *with the proviso that lower alkyamino defined herein is not para-substituted* with *–CH_2NH– when Z is the phenyl ring, (35 U.S.C. 102, 35 U.S.C. 103)*

or a pharmaceutically acceptable salt thereof.

7. A compound of Formula (I) according to claim 1, wherein

X is oxygen,

Y is a direct bond,

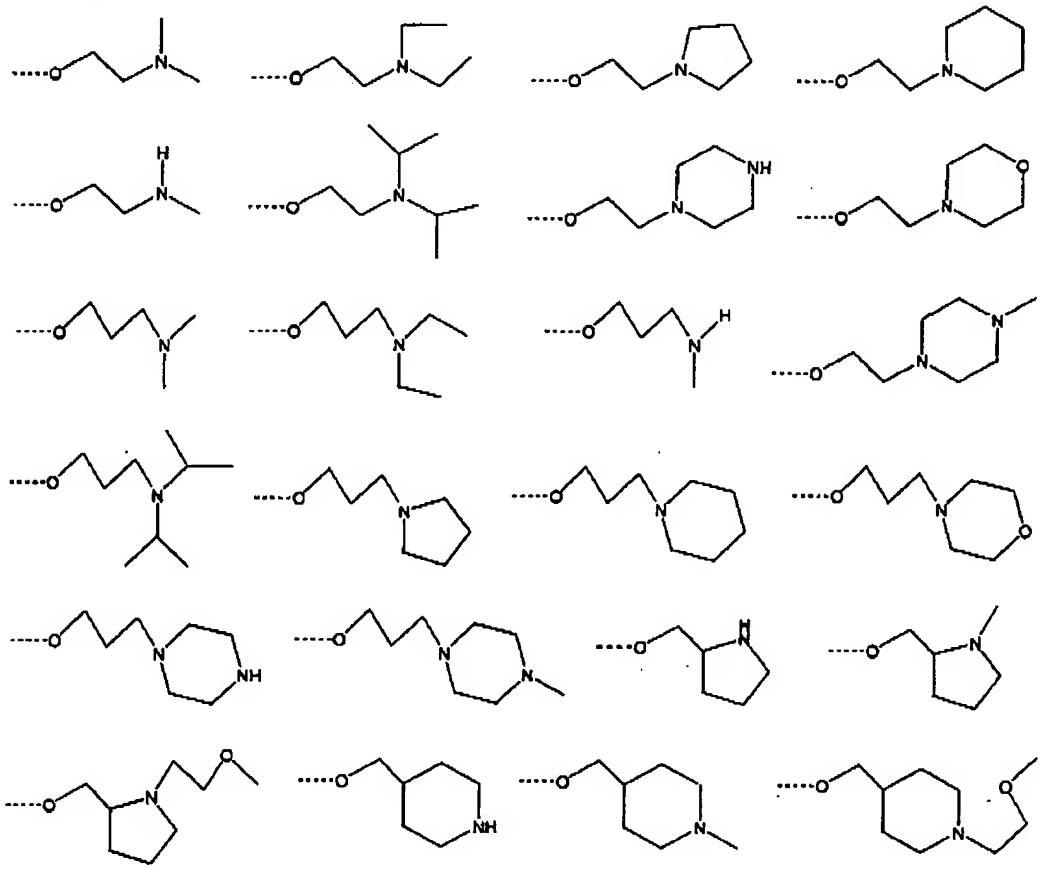
Z is phenyl,

R_1 is: 3-pyridyl or 4-pyridyl

R_2 is: methyl, F, Cl or hydrogen,

R_3 is hydrogen,

R_4 is:

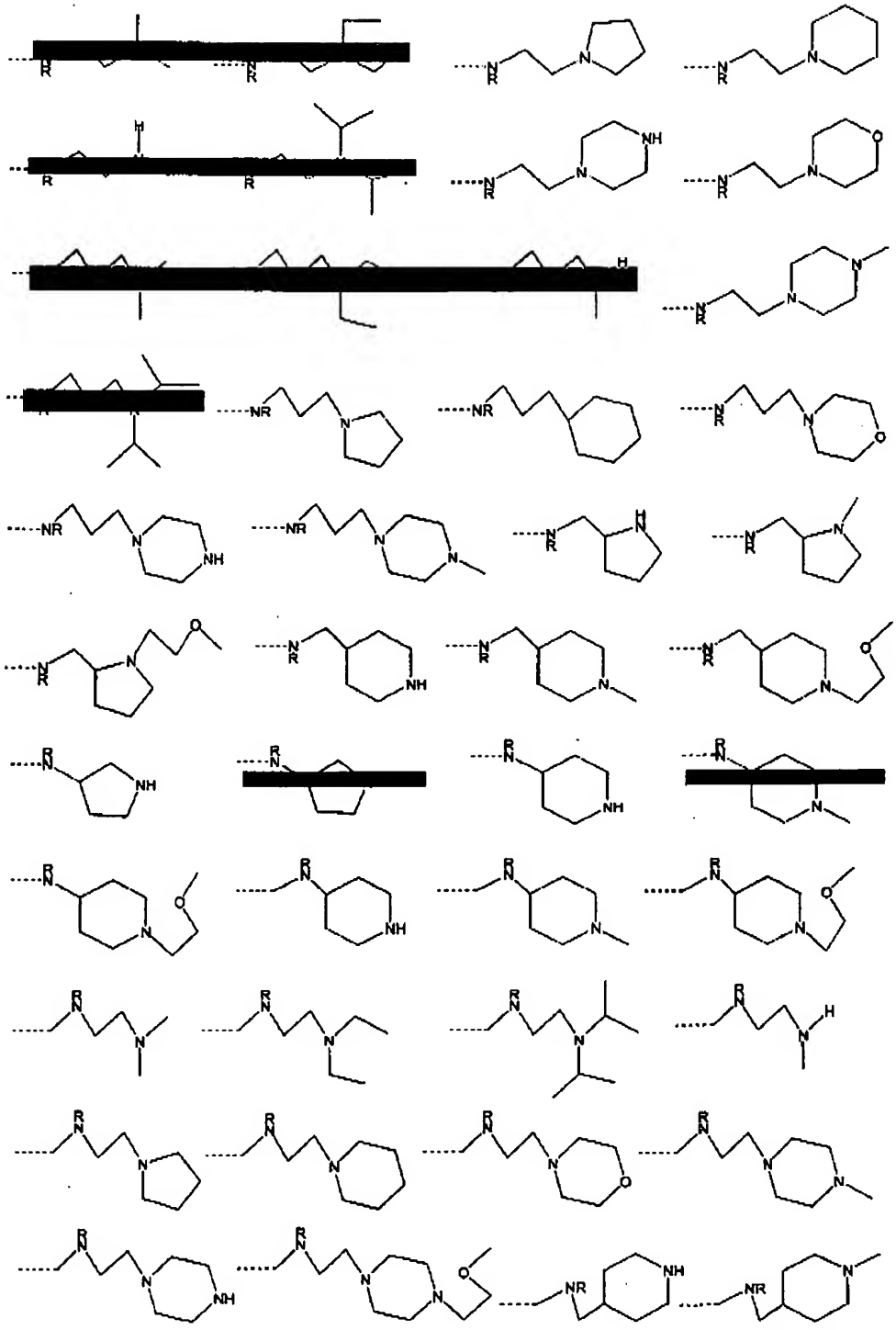


Application Number: 10/821,382

R_4 is (cont'd) :

Application Number: 10/821,382

R_4 is (cont'd) :



(35 U.S.C. 102, 35 U.S.C. 103)

R is hydrogen, lower alkyl, aliphatic, *or* cycloaliphatic ~~or heterocyelyl~~ radicals, *(35 U.S.C. 112)*

or a pharmaceutically acceptable salt thereof.

8. A compound of Formula (I) according to claim 1 is selected from:

[4-(2-aminoethoxy)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)-pyrimidin-2-yl)amino]phenyl}carboxamide

~~N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}{4-[(1-methylpyrrolidin-3-yl)amino]phenyl}carboxamide~~*(35 U.S.C. 102, 35 U.S.C. 103)*

[4-(fluoropiperazinylmethyl)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)-pyrimidin-2-yl)amino]phenyl}carboxamide

N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}-{4-[(1-methylpyrrolidin-2-yl)methoxy]phenyl}carboxamide

N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}[4-(pyrrolidin-3-ylamino)phenyl]carboxamide

[4-(aminofluoromethyl)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}[4-(methylpyrrolidin-3-ylamino)phenyl]carboxamide

{4-[fluoro(4-methylpiperazinyl)methyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

[4-(aminodifluoromethyl)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

~~{4-[methyl(1-methylpyrrolidin-3-yl)amino]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide~~*(35 U.S.C. 102, 35 U.S.C. 103)*

(4-{fluoro[(1-methylpyrrolidin-3-yl)amino]methyl}phenyl)-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

{4-[fluoro(methylpyrrolidin-3-ylamino)methyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

[4-({[2-(dimethylamino)ethyl]amino}fluoromethyl)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

Application Number: 10/821,382

[4-(difluoropiperazinylmethyl)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

{4-[difluoro(4-methylpiperazinyl)methyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

[4-({[2-(dimethylamino)ethyl]amino}difluoromethyl)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

(4-{fluoro[methyl(1-methylpyrrolidin-3-yl)amino]methyl}-phenyl)-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

{4-[fluoro(pyrrolidin-3-ylamino)methyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

{4-[(4-ethylpiperazinyl)difluoromethyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

{4-[(4-ethylpiperazinyl)fluoromethyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

(4-{difluoro[methyl(1-methylpyrrolidin-3-yl)amino]methyl}-phenyl)-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

{4-[difluoro(methylpyrrolidin-3-ylamino)methyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

[4-({[2-(dimethylamino)ethyl]amino}fluoromethyl)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

{4-[difluoro(pyrrolidin-3-ylamino)methyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

(4-{[methyl(1-methylpyrrolidin-3-yl)amino]methyl}phenyl)-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

{4-(methylpyrrolidin-3-ylamino)methylphenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

~~(4-{[(1-methylpyrrolidin-3-yl)amino]methyl}phenyl)-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide~~*(35 U.S.C. 102, 35 U.S.C. 103)*

~~{4-(pyrrolidin-3-ylamino)methylphenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide~~*(35 U.S.C. 102, 35 U.S.C. 103)*

or a pharmaceutically acceptable salt thereof.

Application Number: 10/821,382

9. A pharmaceutical acceptable salt according to any one of claims 1 to 8 is methanesulfonic acid salt.

10. A pharmaceutical composition ~~containing~~ *which comprises as an active ingredient* a compound ~~of formula (I) according to~~ *as defined* in any one of claims 1 to ~~9~~ *8* or a pharmaceutical acceptable salt ~~thereof~~ *of the compound*, or a hydrate or solvate ~~thereof,~~ *of the compound and* ~~together with~~ a pharmaceutical *acceptable* carrier.

[37 CFR 1.75(c), MPEP § 608.01(n)]

~~11. A compound of formula (I) according to any one of claims 1 to 9, or a pharmaceutical acceptable salt thereof, or a hydrate or solvate thereof, for use in a method for the treatment of human or animal cancer.~~ [37 CFR 1.75(c), MPEP § 608.01(n)]